PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

APPLICANT	:	**FARID, A. Hossain, et al.**
SERIAL NO	:	10/662,613
FILED	:	September 15, 2003
TITLE	:	INSULIN-LIKE GROWTH FACTOR-1 RECEPTOR (IGF-1R) POLYMORPHIC ALLELES AND USE OF THE SAME TO IDENTIFY DNA MARKERS FOR REPRODUCTIVE LONGEVITY
Grp./A.U.	:	1634
Examiner	:	KAPUSHOC, Stephen Thomas
Conf. No.	:	2566
Docket No.	:	P05562US00

DECLARATION OF ALAN JOHN MILEHAM
UNDER 37 C.F.R. § 1.132

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

I, Alan John Mileham, hereby declare the following:

1. From 2006 to present I have been the Head of Genomics at Genus.

2. I obtained a Bachelor of Science Honours in Genetics from the University of Leeds in 1977 and a PhD in Molecular Biology from the University of Edinburgh in 1980. From 2000 to 2004 I was the PIC/Sygen Molecular biology Research Manager for PIC International Group and from 2004 to 2006 I was the Laboratory Director for Sygen International. At PIC and Sygen, one aspect of my work focused on providing genetically superior pig breeding stock. Another aspect of our work focused on the identification and association of polymorphic markers with desired traits in pig breeding stock.

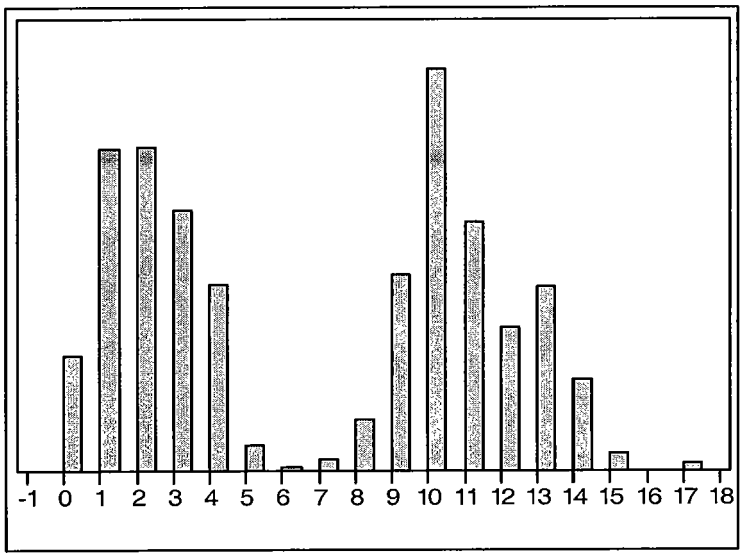
3. A copy of my CV is attached herewith (Exhibit A).

4. I understand that the Examiner has rejected claims 1, 2, 4-10, 25, 26, 45 and 57-63 of the application under 35 U.S.C. § 112, first paragraph on the basis that these claims contain subject matter which is not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

5. This Declaration is submitted herein to demonstrate that the data presented in the first analysis of Example 3 is statistically significant, despite the statement in the specification that the effect on parities is overestimated due to the data structure. In addition, this declaration is also submitted to demonstrate that the data presented in the second analysis of Example 3 is additionally statistically significant.

6. In the first analysis of Example 3 titled "Samples from old surviving sows and from young sows culled during the first 4 parities" 996 sows (972 were successfully genotyped) from four different farms were genotyped and tested for the effect of SNP 3832 on the number of parities. Samples from old surviving sows and from young sows culled during the first 4 parities were used (see figure x1 below).

Figure x1: Distribution of parity.



As illustrated in figure x1, selective genotyping scheme was used in this study, meaning that the high and low extremes of the population were genotyped. When using a selective genotyping scheme, the marker effects are usually overestimated. However, the significance levels (P-values) are correct. Therefore, while it would be expected that the marker effect would be smaller than the 1.11 parities per allele, the P-value of 0.004 is still accurate and highly significant.

7. This declaration additionally presents results from the most recent experiments regarding the analysis titled "Germany (GER): Longevity (reproduction) data from sows with known pedigree with DNA samples from their sires" presented in Example 3. The most recent analysis (August 2007) was conducted by including all available sires that had over 10 daughters and using their most updated phenotypes. Data from 239 sires was used (with records on over 51,000 daughters), 139 of which were line L02 and 100 of which were from L03. Genotypes were collected on the sires, and the phenotype was the sire's estimated breeding value (EBV) for their daughters' age at culling, for sires from L02 and L03. Sires used in the trial had to have at least 10 daughters that completed their lifetime production. The completion of a lifetime production is defined as the daughters either died or were culled. As the experimental design is defined, it is expected that more sires will become available overtime and that the phenotypes (EBV) of old and new sires will continue to change as more siblings and relatives enter and leave the production cycle and affect the sire's EBVs. Therefore repeated analysis using the most recent phenotypes is expected to differ from previous analysis. A significant dominant effect of SNP 3832 was demonstrated in line L02. The '12' genotype had the highest culling-age with dominant effect of 18.9 days and p-value of P=0.053. In L03, however, the marker had no significant additive (p=0.550) or dominant (p=0.832) effects. The lack of consistency between L02 and L03 in this study is not an uncommon occurrence. The fact that different single nucleotide polymorphisms (SNPs) (within the same gene or in different genes) have different effects in different breeds, lines or crosses tends to be the rule rather than the exception, and does not negate the value of this marker when used with appropriate sampling.

8. I hereby declare that all statements made herein of my own knowledge are true, and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application, any patent issuing thereon, or any patent to which this verified statement is directed.

Date: 24th September 2007

Dr. Alan John Mileham

CURRICULUM VITAE

NAME Alan John Mileham

DATE OF BIRTH 13 October 1955

PLACE OF BIRTH Coventry UK

MARITAL STATUS Married to Karen, three children born 1990, 1993 & 1997

EDUCATION
BSc Honours Genetics, University of Leeds 1977
PhD Molecular Biology, University of Edinburgh 1980
Project; cloning genes from bacteriophage T4.

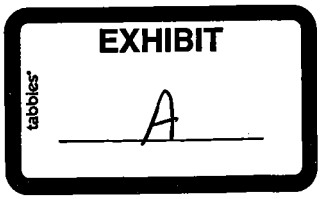
PROFESSIONAL EXPERIENCE
Postdoctoral Associate 1980-1983
University California San Diego and The Agouron Institute, La Jolla California USA
Project; cloning luciferase genes from marine bacteria

Postdoctoral Fellow 1983-1987
Leicester Biocentre, University of Leicester UK
Project; molecular genetics of protein secretion from yeast cells

Senior Scientist 1987-1996
Dalgety plc, Cambridge UK
Projects; development of molecular marker systems in pigs; male reproduction research in pigs, including testis gene expression, semen preservation and semen assessment; shelf life studies on home baking and cooking sauce products.

Group Reproduction Research Manager 1996 – 2000
PIC International Group and University of Cambridge UK
Responsibilities; development of a research team to develop a novel semen sexing system; development of external research collaborations on semen sexing, preservation and assessment; development of an international network on male reproduction; liaison with University of Cambridge and the Department of Pathology.

Molecular Biology Resource Manager 1998 – 2000
PIC International Group and University of Cambridge UK
Responsibilities; management of PIC's molecular biology research workplan and delivery of projects according to agreed timelines; line management of molecular biology team; liaison with University of Cambridge.



PIC Studentship Co-ordinator 1998 – 2000
PIC International Group and University of Cambridge UK
Responsibilities; co-ordination of PIC's CASE studentship programme including project development and selection, student recruitment, liaison with BBSRC, student training, project reporting and organising annual conference.

PIC/Sygen Molecular Biology Research Manager 2000 – 2004
PIC International Group, Berkeley California
Responsibilities; establishment and management of PIC/Sygen's molecular biology research workplan at the Berkeley facility and delivery of projects according to agreed timelines; line management of molecular biology team; liaison with PIC Health Biotechnology and Cambridge groups.

Franklin Laboratory Director 2004 – 2006
Sygen International, Franklin, Kentucky
Responsibilities; establishment and management of Sygen's molecular biology research workplan at the Franklin facility and delivery of projects according to agreed timelines; line management of molecular biology team; liaison with PIC Health Biotechnology and Cambridge groups.

Head of Genomics 2006 – present
Genus, DeForest, Wisconsin
Responsibilities; establishment and management of Genus' genomics research workplan at the DeForest facility and delivery of projects according to agreed timelines; line management of genomics team; member of Genus's senior technology management team.

Principal Publications:

Quilter CR, Blott SC, Wilson AE, Bagga MR, Sargent CA, Oliver GL, Southwood OI, Gilbert CL, Mileham A, Affara NA. Am J Med Genet B Neuropsychiatr Genet. 2007 Oct 5;144(7):862-8. "Porcine maternal infanticide as a model for puerperal psychosis."

Schmutz SM, Berryere TG, Ciobanu DC, Mileham AJ, Schmidtz BH, Fredholm M. Mamm Genome. 2004 Jan;15(1):62-67. "A form of albinism in cattle is caused by a tyrosinase frameshift mutation."

Day AE, Quilter CR, Sargent CA, Mileham AJ. Anim Genet. 2003 Oct;34(5):375-378."Chromosomal mapping, sequence and transcription analysis of the porcine fertilin beta gene (ADAM2)."

Quilter CR, Blott SC, Mileham AJ, Affara NA, Sargent CA, Griffin DK. Mamm. Genome. 2002 Oct;13(10):588-94. "A mapping and evolutionary study of porcine sex chromosome genes."

Day AE, Quilter CR, Sargent CA, Mileham AJ. Anim Genet. 2002 33(3):211-214. "Characterization of the porcine sperm adhesion molecule gene SPAM1- expression analysis, genomic structure, and chromosomal mapping."

Thurston LM, Siggins K, Mileham AJ, Watson PF, Holt WV. Biol Reprod. 2002 66(3):545-54. "Identification of amplified restriction fragment length polymorphism markers linked to genes controlling boar sperm viability following cryopreservation."

Thurston LM, Watson PF, Mileham AJ, Holt WV. J Androl. 2001 (3):382-94. "Morphologically distinct sperm subpopulations defined by Fourier shape descriptors in fresh ejaculates correlate with variation in boar semen quality following cryopreservation."

Short TH, Rothschild MF, Southwood OI, McLaren DG, de Vries A, van der Steen H, Eckardt GR, Tuggle CK, Helm J, Vaske DA, Mileham AJ, Plastow GS, Journal of Animal Science 1997 Dec;75(12):3138-42
"Effect of the estrogen receptor locus on reproduction and production traits in four commercial pig lines."

Mileham AJ, Molecular Biotechnology 1997 Oct;8(2):139-45 "Identification of microorganisms using random primed PCR."

Manger M, Bostedt H, Schill WB, Mileham AJ, Andrologia 1997 Jan-Feb;29(1):9-15 "Effect of sperm motility on separation of bovine X- and Y-bearing spermatozoa by means of free-flow electrophoresis."

Rothschild M, Jacobson C, Vaske D, Tuggle C, Wang L, Short T, Eckardt G, Sasaki S, Vincent A, McLaren D, Southwood O, van der Steen H, Mileham A, Plastow G, Proceedings of the National Academy of Science U S A 1996 Jan 9;93(1):201-5 "The estrogen receptor locus is associated with a major gene influencing litter size in pigs."

Mileham AJ, Methods in Molecular Biology 1995;46:257-67 "Identification of microorganisms using random primed PCR."

Stark MJ, Boyd A, Mileham AJ, Romanos MA Yeast 1990 Jan-Feb;6(1):1-29 "The plasmid-encoded killer system of Kluyveromyces lactis: a review."

Mileham AJ, Siggens KW, Plastow GS, Nucleic Acids Research 1988 Dec 23;16(24):11842 "Isolation of a porcine male specific DNA sequence."

Cohn DH, Mileham AJ, Simon MI, Nealson KH, Rausch SK, Bonam D, Baldwin TO, Journal of Biological Chemistry 1985 May 25;260(10):6139-46 "Nucleotide sequence of the luxA gene of Vibrio harveyi and the complete amino acid sequence of the alpha subunit of bacterial luciferase."

Stark MJ, Mileham AJ, Romanos MA, Boyd A, Nucleic Acids Research 1984 Aug 10;12(15):6011-30
"Nucleotide sequence and transcription analysis of a linear DNA plasmid associated with the killer character of the yeast Kluyveromyces lactis."

Belas R, Mileham A, Simon M, Silverman M, Journal of Bacteriology 1984 Jun;158(3):890-6 "Transposon mutagenesis of marine Vibrio spp."

Mileham AJ, Murray NE, Revel HR, Journal of Virology 1984 May;50(2):619-22 "Lambda-T4 hybrid bacteriophage carrying the thymidine kinase gene of bacteriophage T4."

Cohn DH, Ogden RC, Abelson JN, Baldwin TO, Nealson KH, Simon MI, Mileham AJ, Proceedings of the National Academy of Science U S A 1983 Jan;80(1):120-3 "Cloning of the Vibrio harveyi luciferase genes: use of a synthetic oligonucleotide probe."

Belas R, Mileham A, Cohn D, Hilmen M, Simon M and Silverman M, Science 1982 Nov; 218: 791-793 "Bacterial bioluminescence: isolation and expression of the luciferase genes from vibrio harveyi."

Mileham AJ, Revel HR, Murray NE, Molecular and General Genetics 1980;179(2):227-39 "Molecular cloning of the T4 genome; organization and expression of the frd-DNA ligase region."

Author on 4 US patents as well as numerous patent applications and granted patents worldwide